Cont A3

trace elements comprising at least Mg, K, P and S;
a nitrogen source; and
at least 0.1% (v/v) detergent.

Paragraph beginning on line 29, page 8

A4 Thus, a particularly preferred embodiment of the invention provides a method of culture of mycobacteria, comprising culturing said mycobacteria, in batch fermenter culture or continuous culture, with agitation in the presence of at least 0.1% (v/v) [sufficient] detergent so that a substantially homogenous suspension of single cells is maintained, and in the presence of a growth medium according to combination of the above-described media.

Please amend the claims as follows.

A5 1. (Amended) A method of culture of mycobacteria other than *M. avium*, comprising culturing said mycobacteria, in batch fermenter culture or continuous culture, with agitation and in the presence of [sufficient detergent so that a substantially homogenous suspension of cells is maintained] at least 0.1% (v/v) detergent.

Please cancel claim 2.

3. (Amended) A method according to Claim 1 [or 2], comprising culturing the mycobacteria at a temperature or 35°C +/- 10°C.

4. (Amended) A method according to [any of Claims 1 to 3] Claim 1, comprising maintaining the pH at 6.9 +/- 0.9.

5. (Amended) A method according to [any of Claims 1 to 4] Claim 1, comprising culturing the mycobacteria with an initial dissolved oxygen concentration of at least 1% (v/v) air saturation.

6. (Amended) A method according to [any of Claims 1 to 5] Claim 1, for culture of mycobacteria selected from *M. tuberculosis, M. bovis* and *M. vaccae*.

7. (Amended) A method according to [any of Claims 1 to 6] Claim 1 for batch culture of mycobacteria, wherein detergent is present at from 0.1 to 1.0% (v/v).

8. A method according to Claim 7, wherein detergent is present at about 0.2% (v/v).

9. (Amended) A method according to [any of Claims 1 to 6] Claim 1 for continuous culture of mycobacteria, wherein detergent is present at at least 0.1% (v/v).

10. A method according to Claim 9, wherein detergent is present at at least 0.15% (v/v).

11. (Amended) A method according to Claim 9 [or 10], wherein the culture is carried out continuously with a dilution rate of at least 0.02 h^{-1}.

12. A method according to Claim 11, wherein the culture is carried out continuously with a dilution rate of at least 0.025 h^{-1}.

13. (Amended) A method [of culture of mycobacteria] according to Claim 9, comprising growing said mycobacteria in continuous culture, at a temperature of 35°C +/- 10°C, at a dissolved oxygen tension of at least 1 percent, at a pH of 6.9 +/- 0.9, at a dilution rate of at least 0.02 h^{-1} [and with agitation in the presence of sufficient detergent to maintain a substantially homogenous suspension of single cells].

14. (Amended) A growth medium for culture of mycobacteria, comprising:

a carbon source;

Cont A5

a mitogen;
trace elements comprising at least Mg, K, P and S;
a nitrogen source; and
greater than 0.1% (v/v) detergent.

15. A growth medium according to Claim 14, wherein the carbon source is selected from glucose, glycerol and an amino acid.

16. (Amended) A growth medium according to Claim 14 [or 15], wherein the mitogen is asparagine.

17. (Amended) A growth medium according to [any of Claims 14 to 16] Claim 14, comprising trace elements selected from Ca, Mg, Zn, Co, Cu, Mn, Ni, Fe, K, and mixtures thereof.

18. (Amended) A growth medium according to [any of Claims 14 to 17] Claim 14, wherein the nitrogen source is selected from an amino acid and an ammonium salt.

19. (Amended) A growth medium according to Claim 18, comprising an amino acid component selected from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine and mixtures thereof.

20. (Amended) A growth medium according to [any of Claims 14 to 19] Claim 14, further comprising a vitamin/co-factor component selected from inositol, thiamine, calcium pantothenate, co-enzyme A, nicotinamide, biotin, DL-thiocitic acid, and mixtures thereof.

21. (Amended) A growth medium according to [any of Claims 14 to 20] Claim 14, further comprising one or more components selected from sodium hydroxide, glutathione, glycerol, haemin, sodium pyruvate and ∝-ketoglutarate.

Cont A5

22. (Amended) A method [of culture of mycobacteria] according to Claim 1, comprising culturing said mycobacteria[, in batch or continuous culture, with agitation in the presence of sufficient detergent so that a substantially homogenous suspension of single cells is maintained, and] in the presence of a growth medium [according to any of Claims 14 to 22.] comprising:

a carbon source;
a mitogen;
trace elements comprising at least Mg, K, P and S;
a nitrogen source; and
greater than 0.1% (v/v) detergent.

Please cancel claims 23 and 24.

25. (Amended) A method of culture of a mycobacteriophage, comprising culture of mycobacteria according to [any of Claims 1-13, 22 or 23] Claim 1, and contacting said mycobacteria with a mycobacteriophage.

26. A method according to Claim 25, comprising challenging the mycobacteria with an agent for promoting and/or assisting mycobacteriophage adsorption on the mycobacteria.

27. (Amended) A method according to Claim [25] 26, wherein challenge occurs prior to or substantially at the same time as contacting the mycobacteria with the mycobacteriophage.

28. (Amended) A method according to [any of Claims 25-27] Claim 25, comprising reducing or minimising exposures of the phage to detergent present in the mycobacteria culture medium.

29. (Amended) A method according to Claim 28, comprising allowing phage infection to be established, and then increasing the detergent concentration to an amount sufficient to at least 0.1% (v/v) detergent.

Clean versions of the amended specification and claims is enclosed.

Please charge any fee due to Deposit Account No. 08-2442.

Respectfully submitted,
HODGSON RUSS LLP

By _____
Ranjana Kadle,
Registration No. 40,041

One M & T Plaza, Suite 2000
Buffalo, NY 14203
Tel (716) 848-1628
August 31, 2001
BFLODOCS:587889_1 (CLM901)

CLEAN VERSION OF THE AMENDED SPECIFICATION

Paragraphs starting on line 5, page 4

Accordingly, a first aspect of the invention provides a method of culture of mycobacteria, comprising culturing said mycobacteria, in batch fermenter culture or continuous culture, with agitation and in the presence of at least 0.1% (v/v) detergent. Sufficient detergent is present so that a substantially homogenous suspension of cells is maintained.

Paragraph starting on line 10, page 4

Preferably, the method of the invention comprises growing said mycobacteria in batch fermenter culture or continuous culture, at a temperature of 35°C +/- 10°C, at a dissolved oxygen tension of at least 1.0 percent, at a pH of 6.9 +/- 0.9.

Paragraphs beginning on lines 4, page 8

The invention further provides, in a second aspect, a growth medium for culture of mycobacteria, comprising:

a carbon source;
a mitogen;
trace elements comprising at least Mg, K, P and S;
a nitrogen source; and
at least 0.1% (v/v) detergent.

Paragraph beginning on line 29, page 8

Thus, a particularly preferred embodiment of the invention provides a method of culture of mycobacteria, comprising culturing said mycobacteria, in batch fermenter culture or continuous culture, with agitation in the presence of at least 0.1% (v/v) detergent detergent so that a substantially homogenous suspension of single cells is maintained, and in the presence of a growth medium according to combination of the above-described media.

CLEAN VERSION OF AMENDED CLAIMS

1. (Amended) A method of culture of mycobacteria other than *M. avium*, comprising culturing said mycobacteria, in batch fermenter culture or continuous culture, with agitation and in the presence of at least 0.1% (v/v) detergent.

2. Deleted.

3. (Amended) A method according to Claim 1, comprising culturing the mycobacteria at a temperature or 35°C +/- 10°C.

4. (Amended) A method according to Claim 1, comprising maintaining the pH at 6.9 +/- 0.9.

5. (Amended) A method according to Claim 1, comprising culturing the mycobacteria with an initial dissolved oxygen concentration of at least 1% (v/v) air saturation.

6. (Amended) A method according to Claim 1, for culture of mycobacteria selected from *M. tuberculosis, M. bovis* and *M. vaccae*.

7. (Amended) A method according to Claim 1 for batch culture of mycobacteria, wherein detergent is present at from 0.1 to 1.0% (v/v).

8. A method according to Claim 7, wherein detergent is present at about 0.2% (v/v).

9. (Amended) A method according to Claim 1 for continuous culture of mycobacteria, wherein detergent is present at at least 0.1% (v/v).

10. A method according to Claim 9, wherein detergent is present at at least 0.15% (v/v).

11. (Amended) A method according to Claim 9, wherein the culture is carried out continuously with a dilution rate of at least 0.02 h^{-1}.

12. A method according to Claim 11, wherein the culture is carried out continuously with a dilution rate of at least 0.025 h^{-1}.

13. (Amended) A method according to Claim 9, comprising growing said mycobacteria in continuous culture, at a temperature of 35°C +/- 10°C, at a dissolved oxygen tension of at least 1 percent, at a pH of 6.9 +/- 0.9, at a dilution rate of at least 0.02 h^{-1}.

14. (Amended) A growth medium for culture of mycobacteria, comprising:

a carbon source;
a mitogen;
trace elements comprising at least Mg, K, P and S;
a nitrogen source; and
greater than 0.1% (v/v) detergent.

15. A growth medium according to Claim 14, wherein the carbon source is selected from glucose, glycerol and an amino acid.

16. (Amended) A growth medium according to Claim 14, wherein the mitogen is asparagine.

17. (Amended) A growth medium according to Claim 14, comprising trace elements selected from Ca, Mg, Zn, Co, Cu, Mn, Ni, Fe, K, and mixtures thereof.

18. (Amended) A growth medium according to Claim 14, wherein the nitrogen source is selected from an amino acid and an ammonium salt.

19. (Amended) A growth medium according to Claim 18,

comprising an amino acid component selected from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine and mixtures thereof.

20. (Amended) A growth medium according to Claim 14, further comprising a vitamin/co-factor component selected from inositol, thiamine, calcium pantothenate, co-enzyme A, nicotinamide, biotin, DL-thiocitic acid, and mixtures thereof.

21. (Amended) A growth medium according to Claim 14, further comprising one or more components selected from sodium hydroxide, glutathione, glycerol, haemin, sodium pyruvate and ∝-ketoglutarate.

22. (Amended) A method according to Claim 1, comprising culturing said mycobacteria in the presence of a growth medium comprising:

a carbon source;
a mitogen;
trace elements comprising at least Mg, K, P and S;
a nitrogen source; and
greater than 0.1% (v/v) detergent.

23. (Deleted)

24. (Deleted)

25. (Amended) A method of culture of a mycobacteriophage, comprising culture of mycobacteria according to Claim 1, and contacting said mycobacteria with a mycobacteriophage.

26. A method according to Claim 25, comprising challenging the mycobacteria with an agent for promoting and/or assisting mycobacteriophage adsorption on the mycobacteria.

27. (Amended) A method according to Claim 26, wherein challenge occurs prior to or substantially at the same time as contacting the mycobacteria with the mycobacteriophage.

28. (Amended) A method according to Claim 25, comprising reducing or minimising exposures of the phage to detergent present in the mycobacteria culture medium.

29. (Amended) A method according to Claim 28, comprising allowing phage infection to be established, and then increasing the detergent concentration to an amount sufficient to at least 0.1% (v/v) detergent.